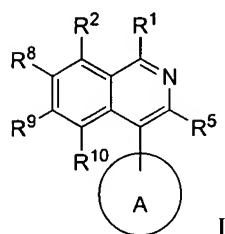


Amendments to the Claims

1. (currently amended) A compound of formula I



or a pharmaceutically acceptable salt, ~~crystal form, or hydrate~~, wherein:

A is

a) an aryl ring selected from phenyl, wherein any stable phenyl aryl ring atom is independently unsubstituted or substituted with

- 1) halogen,
- 2) NO₂,
- 3) CN,
- 4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,
- 5) C≡C R⁴⁶,
- 6) (CRⁱR^j)_rOR⁴⁶,
- 7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),
- 8) (CRⁱR^j)_r C(O)R⁴⁶,
- 9) (CRⁱR^j)_r C(O)OR⁴⁶,
- 10) (CRⁱR^j)_rR⁴⁶,
- 11) (CRⁱR^j)_r S(O)₀₋₂R⁶¹,
- 12) (CRⁱR^j)_r S(O)₀₋₂N(R⁴⁶R⁴⁷),
- 13) OS(O)₀₋₂R⁶¹,
- 14) N(R⁴⁶)C(O)R⁴⁷,
- 15) N(R⁴⁶)S(O)₀₋₂R⁶¹,
- 16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,
- 17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,
- 18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),
- 19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,
- 20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),
- 21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸),

22) oxo,

b) a heteroaryl ring selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, indole, pyrrolopyridine, benzimidazole, benzoxazole, benzothiazole, and benzoxadiazole selected from the group consisting of

~~a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,~~

~~a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and~~

~~a 9 or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,~~

wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with

- 1) halogen,
- 2) NO₂,
- 3) CN,
- 4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,
- 5) C≡C R⁴⁶,
- 6) (CRⁱR^j)_rOR⁴⁶,
- 7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),
- 8) (CRⁱR^j)_r C(O)R⁴⁶,
- 9) (CRⁱR^j)_r C(O)OR⁴⁶,
- 10) (CRⁱR^j)_rR⁴⁶,
- 11) (CRⁱR^j)_r S(O)₀₋₂R⁶¹,
- 12) (CRⁱR^j)_r S(O)₀₋₂N(R⁴⁶R⁴⁷),
- 13) OS(O)₀₋₂R⁶¹,
- 14) N(R⁴⁶)C(O)R⁴⁷,
- 15) N(R⁴⁶)S(O)_xR⁶¹,
- 16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,
- 17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,
- 18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),
- 19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,
- 20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),
- 21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸), or

22) oxo, or

c) a 4-, 5- or 6-membered heterocyclic ring containing 1 or 2 nitrogen atoms, unsubstituted, mono-substituted or di-substituted with C₁-C₆ alkyl;

Y is CH₂, NR⁵³, NC(O)R⁵³, S(O)₀₋₂ or O;

G is H₂ or O;

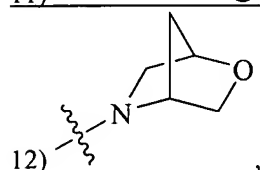
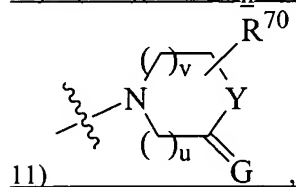
R^a, R^b, ~~R^c~~, ~~R^d~~, ~~R^e~~, ~~R^f~~, ~~R^g~~, ~~R^h~~, Rⁱ, R^j, R^k, and R^l are independently selected from the group consisting of:

- 1) hydrogen,
- 2) C₁-C₆ alkyl,
- 3) halogen,
- 4) aryl,
- 5) R⁸⁰,
- 6) C₃-C₁₀ cycloalkyl, and
- 7) OR⁴,

said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R⁷, disubstituted with R⁷ and R¹⁵, trisubstituted with R⁷, R¹⁵ and R¹⁶, or tetrasubstituted with R⁷, R¹⁵, R¹⁶ and R¹⁷;

R¹ is independently selected from:

- 1) hydrogen,
- 2) halogen,
- 3) CN,
- 4) OR⁴⁰,
- 5) N(R⁴⁰R⁴¹),
- 6) C(O)OR⁴⁰,
- 7) R⁸¹,
- 8) S(O)₀₋₂R⁶,
- 9) N(R⁴⁰)(CR^aR^b)_nR⁶, wherein R⁶ = R⁸³,
- 10) N(R⁴⁰)(CR^aR^b)_nN(R⁴¹R⁴²),



13) $C(O)N(R^{41}R^{42})$, and

14) a 4-, 5-, or 6-membered heterocyclic ring containing 1 nitrogen atom,
unsubstituted, or mono-, di- or tri-substituted with -OH.

1) hydrogen;

2) halogen;

3) NO_2 ;

4) CN ;

5) $CR^{40}=C(R^{41}R^{42})$;

6) $C\equiv CR^{40}$;

7) $(CR^aR^b)_nOR^{40}$;

8) $(CR^aR^b)_nN(R^{40}R^{41})$;

9) $(CR^aR^b)_nC(O)R^{40}$;

10) $(CR^aR^b)_nC(O)OR^{40}$;

11) $(CR^aR^b)_nR^{40}$;

12) $(CR^aR^b)_nS(O)_{0-2}R^6$;

13) $(CR^aR^b)_nS(O)_{0-2}N(R^{40}R^{41})$;

14) $OS(O)_{0-2}R^6$;

15) $N(R^{40})C(O)R^{41}$;

16) $N(R^{40})S(O)_{0-2}R^6$;

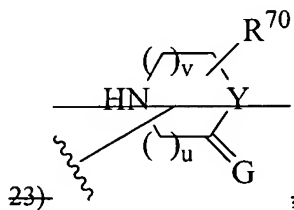
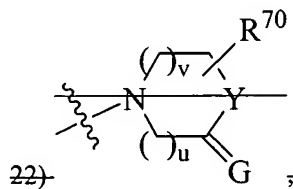
17) $(CR^aR^b)_nN(R^{40})R^6$;

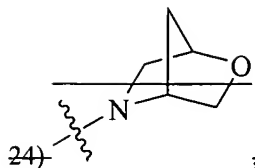
18) $(CR^aR^b)_nN(R^{40})R^6OR^{41}$;

19) $(CR^aR^b)_nN(R^{40})(CR^eR^d)_tC(O)N(R^{41}R^{42})$;

20) $N(R^{40})(CR^aR^b)_nR^6$;

21) $N(R^{40})(CR^aR^b)_nN(R^{41}R^{42})$;





25) $(\text{CR}^a\text{R}^b)_h\text{C}(\text{O})\text{N}(\text{R}^{41}\text{R}^{42})$, and

26) a 4-, 5-, or 6-membered heterocyclic ring containing 1 nitrogen atom, unsubstituted, or mono-, di- or tri-substituted with $-\text{OH}$;

R^2 , R^8 , R^9 -and R^{10} are independently selected from hydrogen and halogen;

R^9 is OCH_3 or OCHF_2 .

1) hydrogen;

2) halogen;

3) NO_2 ;

4) CN ;

5) $\text{CR}^{43}=\text{C}(\text{R}^{44}\text{R}^{45})$;

6) $\text{C}=\text{CR}^{43}$;

7) $(\text{CR}^e\text{R}^f)_p\text{OR}^{43}$;

8) $(\text{CR}^e\text{R}^f)_p\text{N}(\text{R}^{43}\text{R}^{44})$;

9) $(\text{CR}^e\text{R}^f)_p\text{C}(\text{O})\text{R}^{43}$;

10) $(\text{CR}^e\text{R}^f)_p\text{C}(\text{O})\text{OR}^{43}$;

11) $(\text{CR}^e\text{R}^f)_p\text{R}^{43}$;

12) $(\text{CR}^e\text{R}^f)_p\text{S}(\text{O})_{0-2}\text{R}^{60}$;

13) $(\text{CR}^e\text{R}^f)_p\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{43}\text{R}^{44})$;

14) $\text{OS}(\text{O})_{0-2}\text{R}^{60}$;

15) $\text{N}(\text{R}^{43})\text{C}(\text{O})\text{R}^{44}$;

16) $\text{N}(\text{R}^{43})\text{S}(\text{O})_{0-2}\text{R}^{60}$;

17) $(\text{CR}^e\text{R}^f)_p\text{N}(\text{R}^{43})\text{R}^{60}$;

18) $(\text{CR}^e\text{R}^f)_p\text{N}(\text{R}^{43})\text{R}^{60}\text{OR}^{44}$;

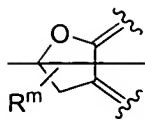
19) $(\text{CR}^e\text{R}^f)_p\text{N}(\text{R}^{43})(\text{CR}^g\text{R}^h)_q\text{C}(\text{O})\text{N}(\text{R}^{44}\text{R}^{45})$;

20) $\text{N}(\text{R}^{43})(\text{CR}^e\text{R}^f)_p\text{R}^{60}$;

21) $\text{N}(\text{R}^{43})(\text{CR}^e\text{R}^f)_p\text{N}(\text{R}^{44}\text{R}^{45})$, and

22) $(\text{CR}^e\text{R}^f)_p\text{C}(\text{O})\text{N}(\text{R}^{43}\text{R}^{44})$;

or R^2 -and R^8 -are independently as defined above, and R^9 -and R^{10} , together with the atoms to which they are attached, form the ring



where R^m is C_{1-6} alkyl;

R^4 , R^{40} , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , R^{47} , R^{48} , R^{49} , R^{50} , R^{51} , R^{52} , and R^{53} are independently selected from:

- 1) hydrogen,
- 2) C_1 - C_6 alkyl,
- 3) C_3 - C_{10} cycloalkyl,
- 4) aryl,
- 5) R^{81} ,
- 6) CF_3 ,
- 7) C_2 - C_6 alkenyl, and
- 8) C_2 - C_6 alkynyl,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{18} , di-substituted with R^{18} and R^{19} , tri-substituted with R^{18} , R^{19} and R^{20} , or tetra-substituted with R^{18} , R^{19} , R^{20} and R^{21} ; R^5 is independently selected from:

- 1) hydrogen,
- 2) halogen,
- 3) CN,
- 4) $C(O)N(R^{49}R^{50})$,
- 5) $C(O)OR^{49}$,
- 6) $S(O)_{0-2}N(R^{49}R^{50})$,
- 7) $S(O)_{0-2}R^{62}$,
- 8) C_1 - C_6 alkyl,
- 9) C_3 - C_{10} cycloalkyl,
- 10) R^{82} ,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{22} , di-substituted with R^{22} and R^{23} , tri-substituted with R^{22} , R^{23} and R^{24} , or tetra-substituted with R^{22} , R^{23} , R^{24} and R^{25} ; R^6 , R^{60} , R^{61} , R^{62} and R^{63} are independently selected from:

- 1) C_1 - C_6 alkyl,
- 2) aryl,
- 3) R^{83} , and
- 4) C_3 - C_{10} cycloalkyl;

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{26} , di-substituted with R^{26} and R^{27} , tri-substituted with R^{26} , R^{27} and R^{28} , or tetra-substituted with R^{26} , R^{27} , R^{28} and R^{29} ;

R⁷, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, and R⁷⁰ are independently selected from:

- 1) C₁-C₆ alkyl,
- 2) halogen,
- 3) OR⁵¹,
- 4) CF₃,
- 5) aryl,
- 6) C₃-C₁₀ cycloalkyl,
- 7) R⁸⁴,
- 8) S(O)₀₋₂N(R⁵¹R⁵²),
- 9) C(O)OR⁵¹,
- 10) C(O)R⁵¹,
- 11) CN,
- 12) C(O)N(R⁵¹R⁵²),
- 13) N(R⁵¹)C(O)R⁵²,
- 14) S(O)₀₋₂R⁶³,
- 15) NO₂, and
- 16) N(R⁵¹R⁵²);

R⁸⁰, R⁸¹, R⁸², R⁸³ and R⁸⁴ are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a 9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting or N, O or S;

n, ~~p, q~~, r, s and t are independently 0, 1, 2, 3, 4, 5 or 6;

u is 0, 1 or 2; and

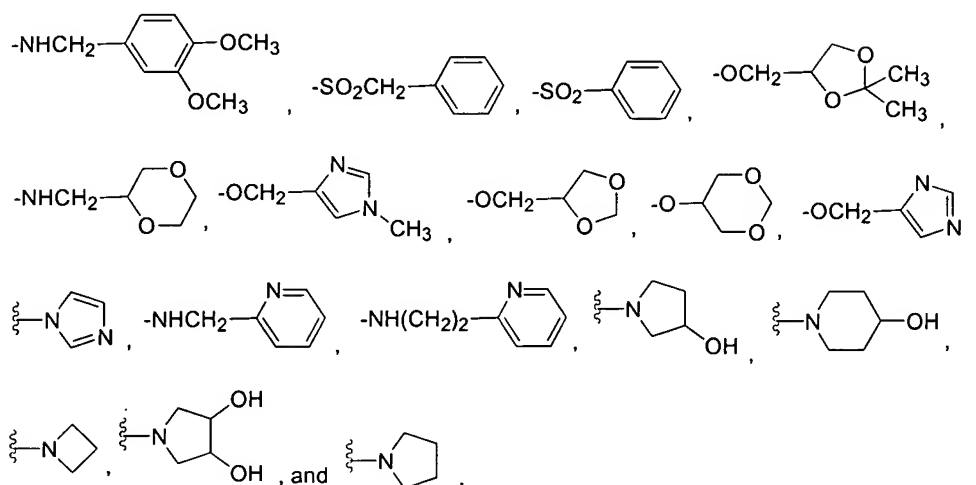
v is 0, 1 or 2.

2.(canceled).

3. (canceled).

4. (original) A compound of Claim 1-3, or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from the group consisting of hydrogen, -SCH₃, -SO₂CH₃, -NH(CH₂)₃OH, -NH(CH₂)₂OH, -NH(CH₂)₂OCH₃,

-NH(CH₂)₃OCH₃, -NH(CH₂)₂NH₂, -NH₂, -SO₂CH₂CH₃, -CN, Cl, -OCH₃,
 -OCH₂CHCH₂, -OCH₂CH(OH)CH₂OH, -NHCH₂CHCH₂, -CH₃, -CH₂CH₂OH,
 -O(CH₂)₂CHCH₂, -O(CH₂)₂CH(OH)(CH₂OH), -NHCH(CH₂OH)₂,
 -NHCH₂CH(OH)CH₂OH, -NH(CH₂)₂CH(OH)CH₂OH,



5. (original) A compound of Claim 4, or a pharmaceutically acceptable salt thereof, wherein A is selected from the group consisting of

- 1) phenyl, wherein any stable ring atom is unsubstituted or substituted with halogen,
- 2) pyridinyl, wherein any stable C ring atom is unsubstituted or substituted with halogen,
- 3) indolyl, wherein any stable C or N ring atom is unsubstituted or substituted with halogen, and
- 4) a heterocyclic ring selected from the group consisting of pyrrolidine, piperidine, piperazine, and azetidine, unsubstituted, mono-substituted or di-substituted with C₁-C₆ alkyl.

6. (original) A compound of Claim 5, or a pharmaceutically acceptable salt thereof, wherein R⁵ is selected from the group consisting of CN and C₁-C₆ alkyl, wherein said alkyl is unsubstituted, mono-substituted with R²², di-substituted with R²² and R²³, tri-substituted with R²², R²³ and R²⁴, or tetra-substituted with R²², R²³, R²⁴ and R²⁵.

7. (original) A compound of Claim 6, or a pharmaceutically acceptable salt thereof, selected from the group consisting of

[(6-methoxy-4-phenylisoquinolin-3-yl)methyl]dimethylamine,

1-(1-chloro-6-methoxy-4-phenylisoquinolin-3-yl)-N,N-dimethylmethanamine,

{[6-methoxy-1-(methylthio)-4-phenylisoquinolin-3-yl]methyl} dimethylamine,
[6-methoxy-1-(methylsulfonyl)-4-phenylisoquinolin-3-yl]methyl(dimethyl)amine oxide,
1-[6-methoxy-1-(methylsulfonyl)-4-phenylisoquinolin-3-yl]-N,N-dimethylmethanamine,
3-[(dimethylamino)methyl]-6-methoxy-4-phenylisoquinoline-1-carbonitrile,
2,3-Dimethyl-6-methoxy-4-phenylisoquinolinium hydroxide,
6-methoxy-1-(2-methoxyethoxy)-3-methyl-4-phenylisoquinoline,
{3-[(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)oxy]propyl}amine,
2-[(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)amino]ethanol,
6-methoxy-3-methyl-1-(methylsulfonyl)-4-phenylisoquinoline,
6-methoxy-N-(2-methoxyethyl)-3-methyl-4-phenylisoquinolin-1-amine,
N-(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)ethane-1,2-diamine,
6-methoxy-3-methyl-4-phenylisoquinoline,
N-(3,4-dimethoxybenzyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1-amine,
6-methoxy-3-methyl-4-phenylisoquinolin-1-amine,
1-(ethylsulfonyl)-6-methoxy-3-methyl-4-phenylisoquinoline,
1-(benzylsulfonyl)-6-methoxy-3-methyl-4-phenylisoquinoline,
6-methoxy-3-methyl-4-phenyl-1-(phenylsulfonyl)isoquinoline,
6-methoxy-3-methyl-4-phenylisoquinoline-1-carbonitrile,
3-tert-butyl-6-methoxy-1-(2-methoxyethoxy)-4-phenylisoquinoline,
1-chloro-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
6-methoxy-4-phenylisoquinoline-1,3-dicarbonitrile,
1-(allyloxy)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-(2,3-dihydroxypropoxy)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(allylamino)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(+/-)-1-[(2,3-dihydroxypropyl)amino]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[(2S)-2,3-dihydroxypropyl]amino}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-{{{(2R)-2,3-dihydroxypropyl}amino}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(+/-)-1-[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-{{{(4S)-2,2-dimethyl-1,3-dioxolan-4-yl}methoxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-{{{(4R)-2,2-dimethyl-1,3-dioxolan-4-yl}methoxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-{{{(2R)-2,3-dihydroxypropyl}oxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-{{{(2S)-2,3-dihydroxypropyl}oxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(+/-)-1-[[2,3-dihydroxypropyl]oxy]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[(3R)-3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[(3S)-3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(+/-)-1-[3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[cis-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
6-methoxy-4-phenyl-1-pyrrolidin-1-ylisoquinoline-3-carbonitrile,
6-methoxy-1-(methylsulfonyl)-4-phenylisoquinoline-3-carbonitrile,
6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1,6-dimethoxy-4-phenylisoquinoline-3-carbonitrile,
1-chloro-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-6-methoxy-1-methylisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-1-[(2-hydroxyethyl)amino]-6-methoxyisoquinoline-3-carbonitrile,
1-amino-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-1-[(3-hydroxypropyl)amino]-6-methoxyisoquinoline-3-carbonitrile,
1-(but-3-enyloxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
(+/-)-1-(2,3-dihydroxypropoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-[(2R)-2,3-dihydroxypropoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
1-[(2S)-2,3-dihydroxypropoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
(+/-)-1-(3,4-dihydroxybutoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
(+/-)-1-[(3R)-3,4-dihydroxybutoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
1-[(3S)-3,4-dihydroxybutoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
(+/-)-1-[(1,4-dioxan-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
1-[(1,4-dioxan-(2R)-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
1-[(1,4-dioxan-(2S)-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
4-(3-fluorophenyl)-6-methoxy-1-[(1-methyl-1H-imidazol-4-yl)methoxy]isoquinoline-3-
carbonitrile,
(+/-)-1-(1,3-dioxolan-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
1-(1,3-dioxolan-(4R)-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
1-(1,3-dioxolan-(4S)-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
1-(1,3-dioxan-5-yloxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-1-{{2-hydroxy-1-(hydroxymethyl)ethyl}amino}-6-methoxyisoquinoline-
3-carbonitrile,
4-(3-fluorophenyl)-1-(1H-imidazol-5-ylmethoxy)-6-methoxyisoquinoline-3-carbonitrile,
1-{{{(2R)-2,3-dihydroxypropyl}amino}}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
1-{{{(2S)-2,3-dihydroxypropyl}amino}}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
(+/-)-1-{{2,3-dihydroxypropyl}amino}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-

carbonitrile,

1-(1H-imidazol-1-yl)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

6-methoxy-4-phenyl-1-[(pyridin-2-ylmethyl)amino]isoquinoline-3-carbonitrile,

6-methoxy-4-phenyl-1-[(2-pyridin-2-ylethyl)amino]isoquinoline-3-carbonitrile,

(+/-)-1-[(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-

carbonitrile,

1-[(3R)-(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-

carbonitrile,

1-[(3S)-(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-

carbonitrile,

1-chloro-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

(+/-)-1-[(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-

carbonitrile,

1-[(2S)-(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-

carbonitrile,

1-[(2R)-(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-

carbonitrile,

(+/-)-6-(difluoromethoxy)-1-{[2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)isoquinoline-

3-carbonitrile,

6-(difluoromethoxy)-1-{[(2S)-2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)isoquinoline-

3-carbonitrile,

6-(difluoromethoxy)-1-{[(2R)-2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)isoquinoline-

3-carbonitrile,

(+/-)-6-(difluoromethoxy)-1-{[2,3-dihydroxypropyl]oxy}-4-(3-fluorophenyl)isoquinoline-

3-carbonitrile,

6-(difluoromethoxy)-1-{{{(2S)-2,3-dihydroxypropyl}oxy}}-4-(3-fluorophenyl)isoquinoline-

3-carbonitrile,

6-(difluoromethoxy)-1-{{{(2R)-2,3-dihydroxypropyl}oxy}}-4-(3-fluorophenyl)isoquinoline-

3-carbonitrile,

1-(4-hydroxypiperidin-1-yl)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-azetidin-1-yl-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

(+/-)-1-[trans-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-[(3R,4R)-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-[(3S,4S)-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile, and

6-methoxy-N-(3-methoxypropyl)-3-methyl-4-phenylisoquinolin-1-amine.

8. (withdrawn)

9. (withdrawn)

10. (withdrawn)

11. (withdrawn)

12. (withdrawn)

13. (withdrawn)

14. (withdrawn)

15. (withdrawn)

16. (withdrawn)

17. (withdrawn)

18. (withdrawn)

19. (currently amended) A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound Claim 1 or a pharmaceutically acceptable salt ~~crystal form or hydrate~~ thereof.

20. (original) A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

21. (withdrawn)

22. (withdrawn)

23. (withdrawn)